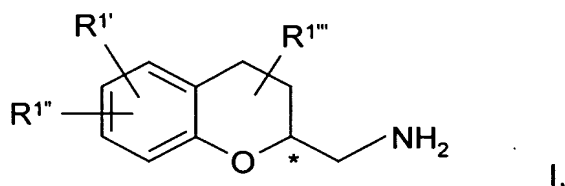


# Patent Claims

1. Process for the preparation of chiral 2-aminomethylchroman derivatives of the formula I



in which the carbon atom labelled with the asterisk is in the (R) or (S) configuration with an enantiomeric excess of > 90% and in which  
 10  $R^{1'}$ ,  $R^{1''}$ ,  $R^{1'''}$  each, independently of one another, denotes H, Hal, A, OA,  $COR^2$ ,  $CH_2R^2$ , NHA,  $NA_2$  or Ar,

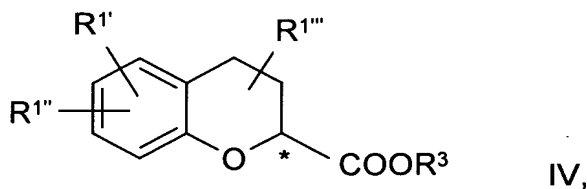
$R^2$  denotes OA or  $NA_2$ ,

A denotes unbranched or branched alkyl having 1-10 C atoms,  
 15 in which one or two  $CH_2$  groups may be replaced by O or S atoms and/or by  $-CH=CH-$  groups and/or in addition 1-7 H atoms may be replaced by F,

Ar denotes unsaturated, partially or fully saturated, mono- or polycyclic homo- or heterocyclic system containing the hetero  
 20 atoms O, N, S which is unsubstituted or mono- or polysubstituted by Hal, A, OA,  $NA_2$  and

Hal denotes F, Cl, Br or I,

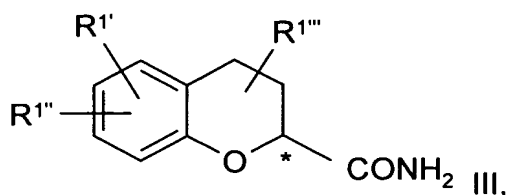
characterised in that an enantiomerically pure (R)- or (S)-chroman-2-carboxylic acid ester of the formula IV



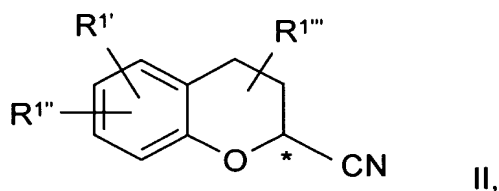
in which

30  $R^3$  denotes methyl, ethyl, 1-propyl, isopropyl, 1-butyl, 2-butyl, isobutyl or allyl

is reacted with ammonia to give a carboxamide of the formula III



which is then dehydrated further to a carbonitrile of the formula II



which is then finally reduced to a compound of the formula I.

2. Process according to Claim 1, in which

- 15
- $R^{1'}$ ,  $R^{1''}$ ,  $R^{1'''}$  each, independently of one another, denotes H, F, A, OA,
- A denotes unbranched or branched alkyl having 1-6 C atoms, and
- $R^3$  denotes methyl or ethyl.

20 3. Process according to Claim 2, in which

- $R^{1'}$ ,  $R^{1''}$ ,  $R^{1'''}$  denote H and
- $R^3$  denotes ethyl.

25 4. Process according to one or more of Claims 1 to 3, characterised in that the chiral carbon atom labelled with the asterisk in the formulae I to IV is in the (R) configuration.

5. Process according to Claim 4, characterised in that the starting material employed is ethyl (R)-chroman-2-carboxylate.

30

6. Process according to one or more of Claims 1 to 5, characterised in that the reagent employed for the preparation of the carbonitrile of the for-

mula II from the carboxamide of the formula III is  $\text{SOCl}_2$ , trifluoroacetic anhydride, cyanuric chloride or trimethylsilyl phosphate.

- 5 7. Process according to one or more of Claims 1 to 6, characterised in that the reducing agent employed for the preparation of the chromanamine of the formula I from the carbonitrile of the formula II is  $\text{LiAlH}_4$  or hydrogen gas with heterogeneous catalysis.
- 10 8. Intermediate compound of the formula III, consisting of (R)-chroman-2-carboxamide and salts and solvates thereof.
9. Intermediate compound of the formula II, consisting of (R)-chroman-2-carbonitrile and salts and solvates thereof.
- 15 10. Process for the preparation of (R)- or (S)-chroman-2-carboxamides of the formula III according to Claim 1 with an enantiomeric excess of  $> 90\%$ , characterised in that an enantiomerically pure (R)- or (S)-chroman-2-carboxylic acid ester of the formula IV according to Claim 1 is reacted with ammonia to give a chroman-2-carboxamide of the formula
- 20 III.

25

30